

**A process for the preparation of acylphosphines**

## Description

5 The present invention relates to a process for the preparation of acylphosphines.

Mono- and bisacylphosphines are known in the state of the art as intermediates which are obtained when preparing mono- and bisacylphosphine oxide or mono- and bisacylphosphine sulfide compounds. These oxides and sulfides find diverse applications as  
10 reactive initiators in the light-induced polymerisation of ethylenically unsaturated compounds.

US 4,298,738 discloses the preparation of monoacylphosphine oxides via reaction of diorganylphosphine chloride with an alcohol and subsequent reaction of the reaction  
15 product with an acid halide. In EP-A 00 40721, monoacylphosphines are obtained from the reaction of acid halides with lithium diorganylphosphine, diorganylphosphine or diorganyltrialkylsilylphosphine.

In Angew. Makromol. Chem. 199 (1992), 1-6, S. Banerjee et al. describe the prepara-  
20 tion of poly(terephthaloylphosphine) via reaction of dilithium phenylphosphine with terephthaloyl chloride.

In Chem. Ber. 92 (1959), 3183-3189, Issleib et al., describe the preparation of acetyl  
25 diphenylphosphine via reaction of sodium diphenylphosphine with acetyl chloride.

US 5,472,992, inter alia, carries out the preparation of bisacylphosphine oxide photo-  
initiators via reaction of the phosphine with the corresponding acid chloride in the pres-  
ence of a base with subsequent oxidation of the bisacylphosphine formed.

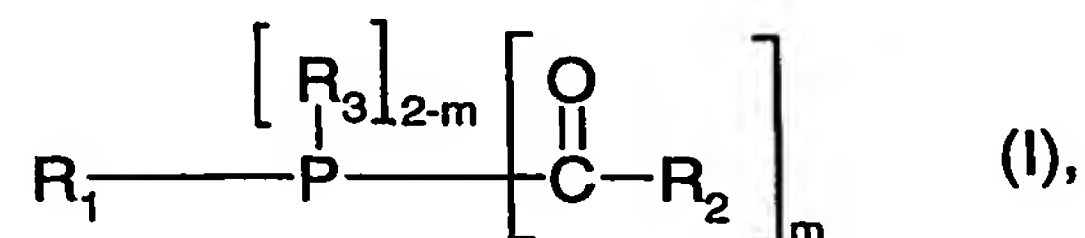
30 As the technology of the mono- and bisacylphosphine oxides is becoming increasingly important owing to the excellent photoinitiator properties of these compounds, there is also a need for highly practicable processes involving as little elaboration as possible for the preparation of the required intermediates, especially of the corresponding mono and bisacylphosphines, but also of the oxide and sulfide end products.

35 WO 00/32612 describes a process by which it is possible to circumvent the use of the phosphine educts ( $R_2\text{-PH}$ ,  $R\text{-PH}_2$ ) which are undesirable because of their volatility, bad smell, toxicity and susceptibility to air and fire. The process is a one-pot process for the preparation of mono- and bisacylphosphines, where the starting material is a monoha-  
40 logenophosphines or a P,P-dihalogenophosphine, which are less volatile, less toxic

and less susceptible to air. The organic phosphorous halides are reacted with an alkali metal in the presence of a catalyst to give a metallised phosphine, which is subsequently reacted with an acid halide to give the acyl phosphine.

- 5 It is an object of the present invention to improve the process described in WO 00/32612.

A process has been found for the preparation of acylphosphines of formula (I)



10

wherein

m is 1 or 2;

- 15  $R_1$  is  $C_1$ - $C_{18}$  alkyl,  $C_2$ - $C_{18}$  alkyl which is interrupted by one or several non-successive O atoms; phenyl-substituted  $C_1$ - $C_4$  alkyl,  $C_2$ - $C_8$  alkenyl, phenyl, naphthyl, biphenyl,  $C_5$ - $C_{12}$  cycloalkyl or a 5- or 6-membered O-, S- or N-containing heterocyclic ring, the radicals phenyl, naphthyl, biphenyl,  $C_5$ - $C_{12}$  cycloalkyl or the 5- or 6-membered O-, S- or N-containing heterocyclic ring  
20 being unsubstituted or substituted by one to five halogen,  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkylthio and/or  $C_1$ - $C_8$  alkoxy;

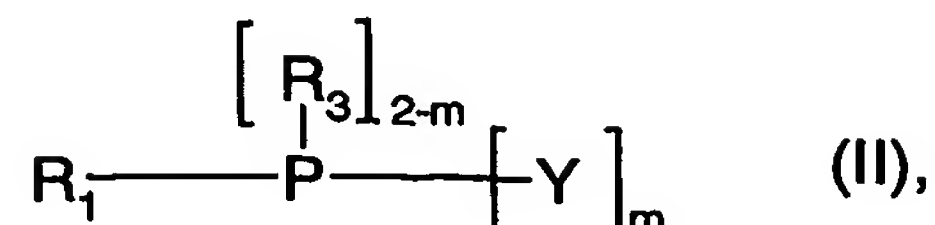
- $R_2$  is  $C_1$ - $C_{18}$  alkyl,  $C_3$ - $C_{12}$  cycloalkyl,  $C_2$ - $C_{18}$  alkenyl, phenyl, naphthyl, biphenyl or a 5- or 6-membered O-, S- or N-containing heterocyclic ring, the radicals  
25 phenyl, naphthyl, biphenyl or 5- or 6-membered O-, S- or N-containing heterocyclic ring being unsubstituted or substituted by one to four  $C_1$ - $C_8$  alkyl,  $C_1$ - $C_8$  alkoxy,  $C_1$ - $C_8$  alkylthio and/or halogen;

- $R_3$  is  $C_1$ - $C_{18}$  alkyl,  $C_2$ - $C_{18}$  alkyl which is interrupted by one or several non-successive O atoms, phenylsubstituted  $C_1$ - $C_4$  alkyl,  $C_2$ - $C_8$  alkenyl, phenyl,  
30 naphthyl, biphenyl,  $C_5$ - $C_{12}$  cycloalkyl or a 5- or 6-membered O-, S- or N-containing heterocyclic ring, the radicals phenyl, naphthyl, biphenyl,  $C_5$ - $C_{12}$  cycloalkyl or the 5- or 6-membered O-, S- or N-containing heterocyclic ring being unsubstituted or substituted by one to five halogen,  $C_1$ - $C_{18}$  alkyl,  $C_1$ - $C_8$  alkylthio and/or  $C_1$ - $C_8$  alkoxy;  
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by

(1) reacting organic phosphorus halides of formula (II)

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wherein  $R_1$ ,  $R_3$  and  $m$  have the meaning cited above;

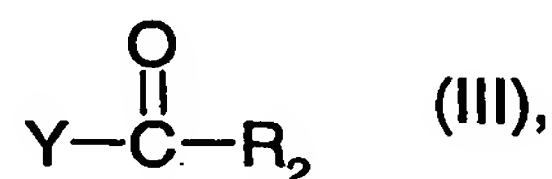
and  $Y$  is Br or Cl,

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with an alkali metal in a solvent in the presence of an activator, wherein the alkali metal is present in the form of a dispersion of alkali metal particles having a mean particle size of  $\leq 500 \mu\text{m}$  in the solvent, and

(2) subsequent reaction with  $m$  acid halides of formula (III)

15



wherein  $R_2$  and  $Y$  have the meaning cited above,

which process is carried out without isolation of the intermediates.

20

$C_1$ - $C_{18}$  Alkyl is linear or branched and is, for example,  $C_1$ - $C_{12}$ -,  $C_1$ - $C_8$ -,  $C_1$ - $C_6$ -, or  $C_1$ - $C_4$ -alkyl. Examples are methyl, ethyl, propyl, isopropyl, n-butyl, sec-butyl, isobutyl, tert-butyl, pentyl, hexyl, heptyl, 2,4,4-trimethylpentyl, 2-ethylhexyl, octyl, nonyl, decyl, undecyl, dodecyl, tetradecyl, pentadecyl, hexadecyl, heptadecyl or octadecyl;  $C_1$ - $C_{12}$ ,  $C_1$ - $C_8$  and  $C_1$ - $C_4$  alkyl are also linear or branched and have, for example, the meanings cited above up to the corresponding number of carbon atoms.

25

$C_2$ - $C_{18}$  Alkyl, which is interrupted once or several times by non-successive -O-, is interrupted, for example, 1-9, e.g. 1-7, 1-5, 1-3 or 1 or 2 times by -O-, the O atoms always being interrupted by at least one methylene group. The alkyl groups may be linear or branched. The structural units obtained are thus, for example,

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$-\text{CH}_2\text{-O-CH}_3$ ,  $-\text{CH}_2\text{CH}_2\text{-O-CH}_2\text{CH}_3$ ,  $-\text{[CH}_2\text{CH}_2\text{O}]_y\text{-CH}_3$ , where  $y = 1$ -8,

$-(\text{CH}_2\text{CH}_2\text{O})_7\text{CH}_2\text{CH}_3$ ,  $-\text{CH}_2\text{-CH(CH}_3\text{)-O-CH}_2\text{-CH}_2\text{CH}_3$  or  $-\text{CH}_2\text{-CH(CH}_3\text{)-O-CH}_2\text{-CH}_3$ .

35

Phenyl-substituted C<sub>1</sub>-C<sub>4</sub>-alkyl is typically benzyl, phenylethyl,  $\alpha$ -methylbenzyl, phenylbutyl or  $\alpha,\alpha$ -dimethylbenzyl, preferably benzyl.

5 C<sub>2</sub>-C<sub>18</sub> Alkenyl radicals may be mono- or polyunsaturated, linear or branched and are, for example, allyl, methallyl, 1,1-dimethylallyl, propenyl, butenyl, pentadienyl, hexenyl or octenyl, preferably allyl. R<sub>2</sub> defined as C<sub>2</sub>-C<sub>18</sub> alkenyl is typically C<sub>2</sub>-C<sub>8</sub>, C<sub>2</sub>-C<sub>6</sub>, preferably C<sub>2</sub>-C<sub>4</sub> alkenyl.

10 C<sub>5</sub>-C<sub>12</sub> Cycloalkyl is, for example, cyclopentyl, cyclohexyl, cyclooctyl, cyclododecyl, preferably cyclopentyl and cyclohexyl, more preferably cyclohexyl; C<sub>3</sub>-C<sub>12</sub> cycloalkyl is additionally e.g. cyclopropyl.

15 C<sub>1</sub>-C<sub>18</sub> Alkoxy is linear or branched radicals and is typically methoxy, ethoxy, propoxy, isopropoxy, n-butyloxy, sec-butyloxy, isobutyloxy, tert-butyloxy, pentyloxy, hexyloxy, heptyloxy, 2,4,4-trimethylpentyloxy, 2-ethylhexyloxy or octyloxy, preferably methoxy, ethoxy, propoxy, isopropoxy, n-butyloxy, sec-butyloxy, isobutyloxy, tert-butyloxy, most preferably methoxy.

20 Halogen is fluoro, chloro, bromo and iodo, preferably chloro and bromo, most preferably chloro.

25 Examples of O-, S- or N-containing 5- or 6-membered heterocyclic rings are furyl, thienyl, pyrrolyl, oxinyl, dioxinyl or pyridyl. The cited heterocyclic radicals may be substituted by one to five, e.g. by one or two, linear or branched C<sub>1</sub>-C<sub>8</sub> alkyl, halogen and/or C<sub>1</sub>-C<sub>8</sub> alkoxy. Examples of such compounds are dimethylpyridyl, dimethylpyrrolyl or methylfuryl.

30 Substituted phenyl, naphthyl or biphenyl is substituted by one to five, e.g. by one, two, three or four, preferably by one, two or three, for example linear or branched C<sub>1</sub>-C<sub>8</sub> alkyl, linear or branched C<sub>1</sub>-C<sub>8</sub> alkoxy or by halogen.

35 Preferred substituents for phenyl, naphthyl and biphenyl are C<sub>1</sub>-C<sub>4</sub> alkyl, preferably methyl, C<sub>1</sub>-C<sub>4</sub> alkoxy, more preferably methoxy, and chloro. Particularly preferred substituents are, for example, 2,4,6-trimethylphenyl, 2,6-dichlorophenyl, 2,6-dimethylphenyl or 2,6-dimethoxyphenyl.

R<sub>2</sub> is, for example, phenyl, preferably 2,4,6-trimethylphenyl, 2,6-dimethylphenyl or 2,6-dimethoxyphenyl, most preferably 2,4,6-trimethylphenyl.

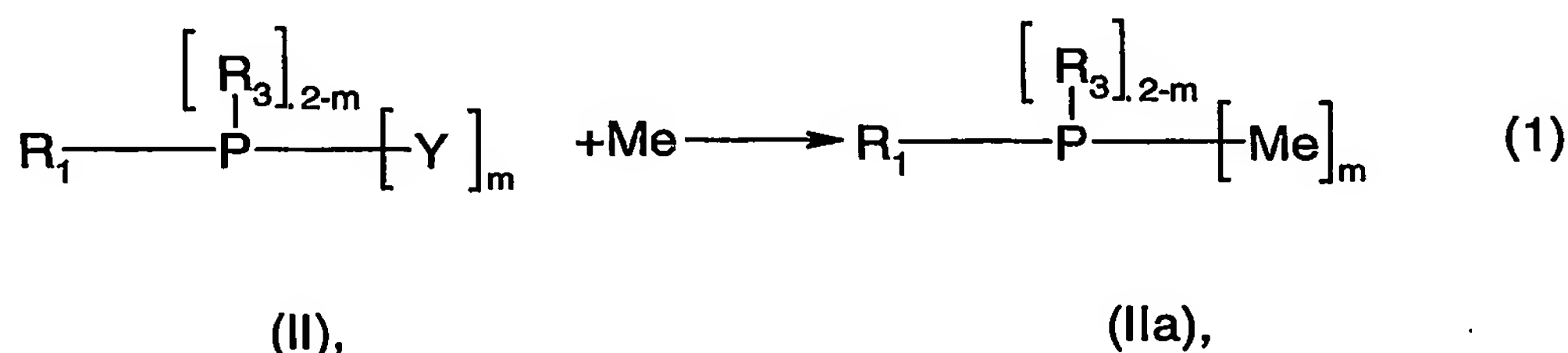
$R_1$  and  $R_3$  are preferably unsubstituted phenyl or  $C_1$ - $C_4$  alkyl substituted phenyl, most preferably phenyl.

$C_1$ - $C_4$  Alkoxyphenyl is phenyl which is substituted by one to four alkoxy radicals, for example 2,6-dimethoxyphenyl, 2,4-dimethoxyphenyl, methoxyphenyl, ethoxyphenyl, propoxyphenyl or butoxyphenyl.

Within the scope of the present description and claims, "and/or" shall mean that not only one of the defined alternatives (substituents) may be present, but that also several different ones of the defined alternatives (substituents) may be present together, i.e. mixtures of different alternatives (substituents).

Within the scope of the present description and claims, "at least" shall be defined as "one" or "more than one", for example one or two or three, preferably one or two.

In the process of the invention for the preparation of mono- and bisacylphosphines, an organic phosphorus halide (II) is first reacted with an alkali metal, the metallised phosphine (IIa) being formed via different intermediary steps:



$R_1$ ,  $R_3$  and  $m$  have the meaning cited above, Me is an alkali metal.

Suitable alkali metals are, for example, lithium, sodium or potassium. It is also possible to use mixtures of these metals in the process of this invention. If lithium, sodium or potassium are used, then it is useful to employ from 4 to 8 atom equivalents of the alkali metal for the preparation of bisacylphosphines, and 2 to 4 atom equivalents of the alkali metal for the preparation of monoacylphosphines.

In a preferred embodiment of the process of the invention, sodium is used as the alkali metal.

The reaction (1) of the organic phosphorous halide with the alkali metal is carried out in a solvent. Suitable solvents are known aliphatic or aromatic solvents. Suitable solvents



are, for example, alkanes such as pentane, hexane, petroleum ether and ligroine, cycloalkanes such as cyclohexane and decalin, aromatic hydrocarbons such as toluene, ethyl benzene and tetralin, aliphatic, aromatic and mixed aliphatic-aromatic ethers, such as dimethyl ether, diethyl ether, methylpropyl ether, 1,2-dimethoxyethane, bis(2-methoxyethyl) ether, dibutylether, methylphenylether and cyclic ethers, such as tetrahydrofuran and dioxane. Toluol and ethyl benzene are preferably used. The reaction temperatures are preferably in the range from -20°C to +160°C, e.g. from 80°C to 120°C.

It is an essential feature of the process of the invention that the alkali metal Me is present in the reaction medium in the form of particles having a mean particle size of  $\leq 500 \mu\text{m}$ , preferably  $\leq 200 \mu\text{m}$ , more preferably  $\leq 50 \mu\text{m}$  when reaction (1) is carried out. The lower limit for the mean particle size of the alkali metal particles is generally about  $1 \mu\text{m}$ , preferably  $5 \mu\text{m}$ , more preferably  $10 \mu\text{m}$ . Alkali metal particles having the specified mean particle size can be readily produced by dispersing molten alkali metal in the reaction medium by means of a dispersing apparatus, preferably a turbine stirrer or a reaction mixing pump. A dispersion of alkali metal in the solvent is prepared in a suitable manner by adding alkali metal to a solvent, which is one or more of the solvents listed above, heating the mixture to a temperature above the melting point of the alkali metal, and vigorously stirring the mixture with a high speed turbine stirrer. The temperature employed while dispersing the alkali metal in the solvent is in general  $\geq 95^\circ\text{C}$ , for example from  $95^\circ\text{C}$  to  $200^\circ\text{C}$  for sodium,  $\geq 64^\circ\text{C}$ , for example from  $64^\circ\text{C}$  to  $200^\circ\text{C}$  for potassium and  $\geq 180^\circ\text{C}$ , for example from  $180^\circ\text{C}$  to  $250^\circ\text{C}$  for lithium. A stable dispersion is obtained, which can be cooled and kept below the melting point of the alkali metal. In one embodiment of the inventive process, the alkali metal dispersion is prepared separately, cooled and subsequently transferred to a reaction vessel where it is reacted with the organic phosphorous halide to give the metallised phosphine (IIa).

The reaction (1) of the organic phosphorous halide with the alkali metal is carried out in the presence of an activator. Suitable activators are aliphatic alcohols having 1 to 10 carbon atoms, preferably ethanol, 1-propanol, 2-propanol, n-butanol, iso-butanol, sec.-butanol and tert.-butanol, more preferably n-butanol, aromatic chlorohydrocarbons, preferably chlorobenzene, aliphatic chlorohydrocarbons, preferably 1-chloropentane, aromatic bromohydrocarbons, preferably bromobenzene, and aliphatic bromohydrocarbons. Two or more different activators may be employed, which may be added at different stages of the reaction. Most preferred activators are n-butanol and chlorobenzene.

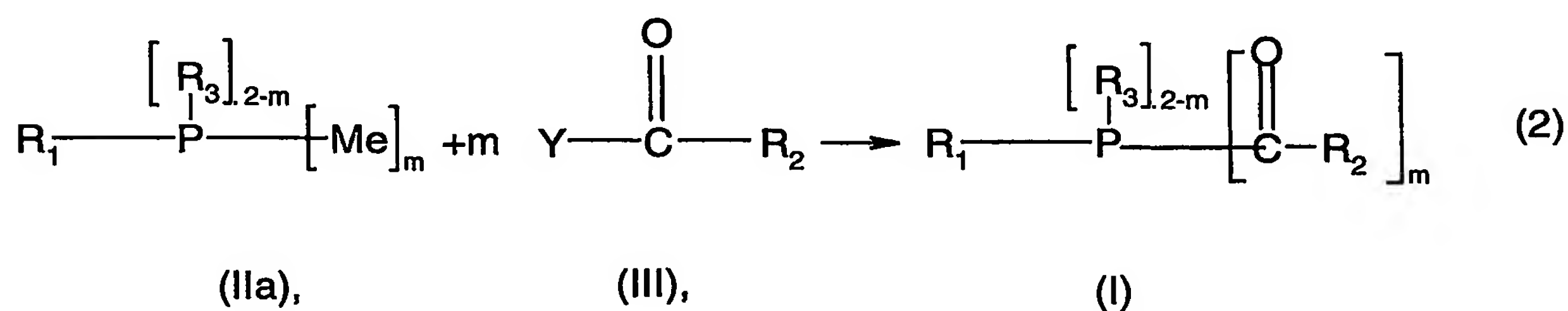
Each activator is present in the reaction mixture in an amount of 0,01 to 20 mol.-% based on the amount of the alkali metal.

If chlorobenzene or 1-chloropentane is employed as an activator, it is added in an amount of in general from 0,1 to 20 mol-%, preferably from 1 to 10 mol-%, more preferably from 3 to 7 mol-%, based on the amount of the alkali metal. If an aliphatic alcohol is used as an activator, it is added in an amount of in general from 0,01 to 10 mol-%, preferably from 0,05 to 1 mol-%, based on the amount of the alkali metal.

Usefully, the organic phosphorous halide, optionally dissolved in a solvent which can be one or more of the solvents listed above, is added continuously to the alkali metal dispersion in the presence of the activator. Additional activator may be added at a later stage of the reaction. In a particularly preferred embodiment of the inventive process, sodium is employed as the alkali metal, and chlorobenzene and n-butanol are used as activators, in the amounts specified above. Chlorobenzene is present as a first activator in the alkali metal dispersion when the addition of the organic phosphorous halide starts. The organic phosphorous halide is added until the reaction stops to develop heat. At this point, n-butanol is added as a second activator, and the addition of organic phosphorous halide is continued. The reaction again starts to develop heat after the addition of the second activator, and the reaction continues to proceed. The n-butanol can be added all at once or in a continuous manner along with the organic phosphorous halide.

The metallised phosphine (IIa) obtained as described above is reacted in the next reaction step (2) with an acid halide (III) to the mono- or bisacylphosphine (I):

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R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, Me and m have the meaning cited above. Y is bromo or chloro, preferably chloro.

The solvents used may be, for example, the same as those used above for the first step. However, it is also possible to remove the solvent used in the first step by distillation and to take up the residue in another solvent and then to further process it.

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It is preferred to work in the same solvent as in the preceding step, most preferably in toluene or ethylbenzene

5 The reaction temperatures for the reaction with the acid halide are usefully in the range from -20 to +120°C.

10 The mono- or bisacylphosphine of formula (I) can be isolated by the customary technological methods which are known to the skilled person, for example by evaporation or distillation of the solvents and/or crystallisation. Likewise, the customary methods of purification may be used, for example crystallisation, distillation or chromatography. Usefully, water is added to the reaction mixture in order to remove sodium chloride, the water phase is separated off and the product is isolated from the organic phase by distilling off the solvents and/or by crystallisation of the product. The product can be further purified in the usual manner, for example by recrystallisation from a suitable solvent.  
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However, the phosphines can also be reacted without isolation to the corresponding mono- or bisacylphosphine oxides or mono- or bisacylphosphine sulfides.

20 Depending on the substituents used, isomeric mixtures may be formed by the process of the invention.

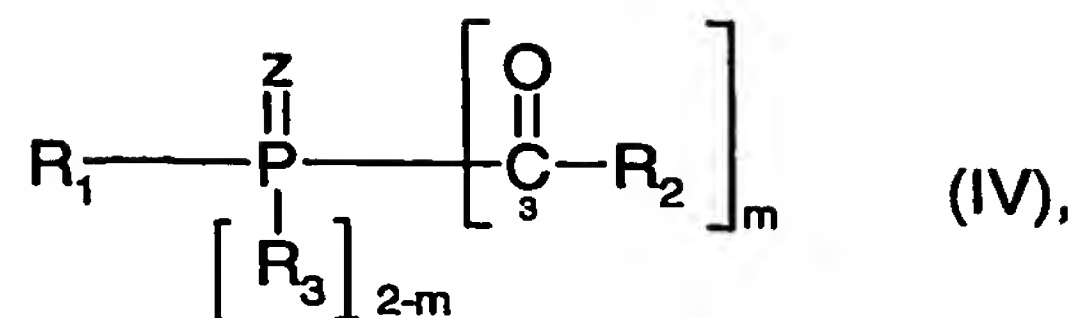
Using the process of this invention it is also possible to prepare mono- and bisacylphosphines together in one reaction step.  
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By means of the process of the invention it is furthermore also possible to prepare mixtures of aliphatic and aromatic monoacylphosphines or mixtures of aliphatic and aromatic bis-acylphosphines. Mixtures of compounds of formula (II), wherein  $R_1$  is an aliphatic radical, and of compounds of formula (II), wherein  $R_1$  is an aromatic radical, are used in this case.  
30

The acid halides (III) used as starting materials are known substances, some of which are commercially available, or may be prepared in analogy to known compounds.

35 From the acylphosphine of formula (I) obtained in reaction (2), acylphosphine oxides and acylphosphine sulfides of formula (IV)





wherein

$R_1$ ,  $R_2$ ,  $R_3$  and  $m$  have the meaning cited in claim 1, and

5  $Z$  is O or S,

can be prepared by oxidation or reaction with sulfur of the acylphosphine of formula (I).

10 The preparation of acylphosphine oxides and acylphosphine sulfides from the acylphosphines of the formula (I) is described in detail in WO00/32612.

The following Examples illustrate the invention in more detail.

#### Examples

15

##### Example 1: Preparation of bis-(2,4,6-trimethylbenzoyl)-phenylphosphine

(Activation by chlorobenzene and n-butanol, stirrer-type: turbine stirrer)

20 Under an inert atmosphere and with exclusion of moisture a dispersion of sodium (11.5 g; 0.50 mol) in toluene (100 ml) is produced by stirring with a high speed turbine stirrer with 11000 rpm at 105 °C resulting in sodium with a main particle size of less than 50 µm. The mixture is cooled to 30-35°C without stirring. Then the turbine stirrer is started again and chlorobenzene (2.8 g; 0.025 mol) is added dropwise and the contents of the  
25 flask warms to 45-50°C. The resulting black suspension is heated to 100°C and P,P-dichlorophenylphosphine (19.7 g, 0.11 mol) is added dropwise at this temperature with exothermic behaviour. After the addition of ¼ of the whole amount of P,P-dichlorophenylphosphine the reaction stops to develop heat. At this point n-butanol (0.05 ml) is added and the exothermic reaction starts again. All the rest of the addition  
30 of P,P-dichlorophenylphosphine stays exothermic. The resulting green suspension is stirred at 100-110°C for 30 min. The mixture is cooled to 75°C and 2,4,6-trimethylbenzoylchloride (43.8g; 0.24 mol) is added dropwise over a period of 30 min at this temperature. An exothermic reaction was observable. To the brown suspension was added toluene (200 ml) and the mixture was stirred for 60 min at 70-85°C. The  
35 mixture was hydrolysed with water (150 ml) and the phases were separated. The prod-

uct phase was analysed by  $^{31}\text{P}$ -NMR. This showed the desired bis-(2,4,6-trimethylbenzoyl)-phenylphosphine with 85-90% purity.

Comparative example 1: Preparation of bis-(2,4,6-trimethylbenzoyl)-phenylphosphine

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(Activation by chlorobenzene and n-butanol, stirrer-type: standard blade stirrer)

Under an inert atmosphere and with exclusion of moisture a dispersion of sodium (11.2 g, 0.50 mol) in toluene (200 ml) is produced by stirring with a standard blade stirrer with 1500 rpm at 105 °C resulting in sodium with a main particle size of 950 µm. The mixture is cooled to 30-35°C without stirring. Then the stirrer is started again with 300 rpm and chlorobenzene (2.93 g, 0.026 mol) is added dropwise without any visible effects. Then n-butanol (0.1 ml) is added and the mixture is heated to 40-50°C leading to a black coloured suspension. This suspension is heated to 100°C and P,P-dichlorophenylphosphine (20.4 g, 0.114 mol) is added dropwise at this temperature with exothermic behaviour. After the addition of ¼ of the whole amount of P,P-dichlorophenylphosphine the reaction stops to develop heat. At this point n-butanol (0.05 ml) is added and the exothermic reaction does not start again. The addition of n-butanol (0.05 ml) is repeated and the exothermic reaction starts again. All the rest of the addition of P,P-dichlorophenylphosphine stays exothermic. The resulting brown suspension is stirred at 95-105°C for 60 min. The mixture is cooled to 75°C and 2,4,6-trimethylbenzoylchloride (45.85 g, 0.251 mol) is added dropwise over a period of 30 min at this temperature. An exothermic reaction was observable only for the first 10% of the total amount of 2,4,6-trimethylbenzoylchloride. The suspension is stirred at 90°C for 90 min. The mixture was hydrolysed with water (200 ml) and the phases were separated. The product phase was analysed by  $^{31}\text{P}$ -NMR. This showed the desired bis-(2,4,6-trimethylbenzoyl)-phenylphosphine only in traces (ca. 1%).

Example 2: Preparation of bis-(2,4,6-trimethylbenzoyl)-phenylphosphine oxide

(Activation only by n-butanol, stirrer-type: turbine stirrer)

Under an inert atmosphere and with exclusion of moisture a dispersion of sodium (11.5 g, 0.50 mol) in toluene (100 ml) is produced by stirring with a high speed turbine stirrer at 105 °C. With further stirring at 100°C, n-butanol (0.05 ml) is added. To the resulting grey suspension is added P,P-dichlorophenylphosphine (21.5 g, 0.12 mol) dropwise over a period of 20 min with constant development of exothermic heat. The mixture is then stirred for 30 min at 100-110°C and toluene (100 ml) was added. Then 2,4,6-trimethylbenzoylchloride (49.3 g, 0.27 mol) was added dropwise over a period of 30

min at 70-80°C. Only during the first 20% of the addition of 2,4,6-trimethylbenzoylchloride an exothermic reaction is observable. The reaction temperature is increased to 85°C and later to 110°C so to allow the exothermic reaction. The mixture is stirred at 110°C for 30 min. The temperature is lowered to 40°C and H<sub>2</sub>O<sub>2</sub> (30%, 17.0 g, 0.15 mol) and water (150 ml) are added dropwise. The reaction is stirred at a temperature between 40 and 60°C for 2 h. The phases were separated. The product phase was analysed by <sup>31</sup>P-NMR. This showed the desired bis-(2,4,6-trimethylbenzoyl)-phenylphosphine oxide with 25% purity.